Review Article

Should low-dose computed tomography kidneys, ureter and bladder be the new investigation of choice in suspected renal colic?: A systematic review

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ABSTRACT

Introduction: Computed tomography kidneys, ureter and bladder (CTKUB) is the accepted gold standard investigation for suspected renal colic. Dose considerations are particularly pertinent in the context of detecting urolithiasis given the high risk of disease recurrence, which can necessitate multiple radiological examinations over the lifetime of a stone-former. We performed a systematic review of the literature to see whether there was any evidence that reducing the effective radiation dose of a CTKUB compromised the diagnostic accuracy of the scan.

Materials and Methods: Relevant databases including MedLine, EMBASE, DARE and the Cochrane Library were searched from inception to October 2012. All English language articles reporting on prospective studies where non-contrast, low-dose CT (LDCT) was used to investigate adults (males and non-pregnant females) presenting with flank pain or suspected urolithiasis were included. LDCT was defined as an effective radiation dose <3 mSv per examination.

Results: Our initial search identified 497 records. After removing duplicates, 390 abstracts were screened, of which 375 were excluded, principally because outcomes of interest were not presented. Six papers remained for the final analysis, reporting on a total of 903 patients. Individual studies showed a prevalence of urolithiasis ranging between 36% and 88%, with additional pathologies found in 5-16%. The effective radiation dose of the LDCT techniques used ranged from 0.5 to 2.8 mSv. The sensitivity of LDCT for diagnosing stone disease was 90-97% with a specificity of 86-100%.

Conclusions: The sensitivity and specificity of CTKUB for diagnosing urolithiasis remains high, even when the effective radiation dose is lowered. LDCT may miss some small stones (<3 mm), especially in obese patients (>30 kg/m^2), but in this group LDCT still identifies most alternative diagnoses. With at least one level 1A and two level 1B studies supporting the use of LDCT, there is Grade A recommendation for its use as the first-line investigation in suspected renal colic in non-obese patients.

Key words: Computed tomography of the renal tract, low-dose computed tomography, renal colic, renal stones, urolithiasis

INTRODUCTION

In accordance with both the British Association of Urological Surgeons referral guidelines[1] and the European Association of Urology Guidelines,[2] computed tomography (CT) of the renal tract (Computed tomography kidneys, ureter and bladder [CTKUB]) is now accepted as the gold standard investigation in suspected renal colic. Prior to this, plain radiographs of the abdomen including the KUB ± functional imaging in the form of intravenous urography (IVU) were the investigations of choice in patients presenting with acute flank pain or suspected urolithiasis. The advantage of CT is that most stones will be detected regardless of size, composition and location. The main exception to this is the indinavir stone, which can form in patients being treated for the human immunodeficiency virus.

Even though it is a more sensitive investigation[3-5] and has the advantage of being able to detect the alternative diagnoses[6,7] there are concerns regarding the level of radiation exposure with a CT scan.[2] However, in recent years there have been advancements within the field of CT that mean it is now possible to acquire cross-sectional images at a much lower effective radiation dose, generally less than 3 mSv per

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examination. Dose considerations are particularly pertinent in the context of detecting urolithiasis given the high risk of disease recurrence, which can necessitate multiple radiological examinations over the lifetime of a stone former, making the individual radiation doses received during each examination of greater concern. Much of this concern arises from the knowledge that the overall lifetime attributable risk of developing cancer is generally 1 in 200 for every 100 mSv of radiation exposure[8] and the International Commission on Radiological Protection recommend a yearly dose limit for occupational radiation exposure of 50 mSv. However, there is always a risk that with reducing the radiation, image quality may be compromised, given that the clarity of radiographic images is inversely proportional to the amount of radiation used in milliamperes.[9] We performed a systematic review of the literature to see whether there was any evidence that reducing the effective radiation dose of a CTKUB compromised the image quality and subsequent diagnostic accuracy of the scan.

MATERIALS AND METHODS

Search strategy

This systematic review was performed according to the Cochrane diagnostic accuracy reviews guidelines and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.[10]

The Cochrane Library, Medline, EMBASE and DARE databases were searched for English language publications from 1990 to October 2012 using the following terms: Renal colic, ureter* colic, ureteral calculi, urinary calcul*, kidney calcul*, flank pain, computed tomograph*, X-ray CT, spiral CT, CT scan, low dose and radiation dosage. Boolean operators (and, or) were also used in succession to narrow and broaden the search.

Study selection

Two reviewers (TD and NJ) identified all studies that appeared to fit the inclusion criteria for full review. Each reviewer independently selected studies for inclusion in the review. Disagreement between the two extracting authors was resolved by consensus. If consensus between the two reviewers could not be reached, a third author (BS) was deferred to for arbitration and consensus.

The first step in study selection was the exclusion of duplicate reports. The title and abstract of the papers identified by the search were then examined and any studies, which were obviously irrelevant, were excluded at this stage. The full text of each of the remaining studies was then reviewed for eligibility and all relevant information and data extracted.

Data extraction and quality assessment

The objectives were to evaluate the diagnostic accuracy of low-dose CTKUB in detecting urolithiasis. Low-dose CT (LDCT) was defined as an effective radiation dose <3 mSv.[11]

The following variables were extracted from each eligible study: First author, title, year and journal of publication, number of patients studies, population demographics (including gender, age and details of weight and/or body mass index (BMI)), details of low-dose imaging technique and reference standard used (including effective radiation doses), stone detection rate and detection of alternative diagnoses. Disagreement between the extracting authors was resolved by consensus or referred to the senior author (BS).

Quality evaluation

Each study identified for inclusion in the systematic review was appraised for methodology using the "QUADAS tool."[12] Levels of evidence and recommendation were based on the Centre for Evidence Based Medicine (CEBM).[13]

RESULTS

Literature search

Searching the 4 databases identified a total of 497 articles. Of these articles, 107 were duplicates and were subsequently excluded. Titles and abstracts for the remaining 390 articles were reviewed for eligibility by applying the inclusion and exclusion criteria outlined are shown in Table 1. A further 375 articles were excluded at this stage, principally because outcomes of interest were not presented. Full text review of the remaining 15 articles was performed, resulting in the identification of 6 papers for inclusion in the systematic review [Figure 1].

Characteristics of the included studies

Six papers were included, reporting on a total of 903 patients[14-19] [Table 2]. The study population was composed of patients aged 15-90 years, with a reported

Table 1: Selection criteria for studies

Inclusion criteria	Exclusion criteria
Prospective studies of an adult population presenting with flank pain or suspected urolithiasis	Cadaveric studies Retrospective studies
Low dose CT (index test) performed on all patients	Simulated studies Contrast enhanced CT studies
Reference test (SDCT, or a combination of imaging and clinical follow-up) performed on all patients who had a LDCT	Studies with unclear definition of a standard Case control studies Studies involving pregnant patients

CT=Computed tomography, KUB=Kidneys, ureter and bladder, SDCT=Standard-dose CTKUB, LDCT=Low-dose CTKUB

Table 2: Table of the included studies

Study	Study type level of evidence	Number of patients	Prevalence of urolithiasis %	Prevalence of other diagnoses %	Population
Kim *et al*. 2005[14]	Prospective comparative 1B	121	87.9	7.4	M: 79, F: 42 Age: 19-86 (mean 44 years)
Poletti *et al*. 2007[15]	Prospective comparative 1B	125	80.8	4.8	M: 87, F: 38 Age: 19-80 (mean 45 years) BMI<18.5=9% BMI 18.5-24.9=27% BMI 25-29.9=10% BMI>30=10%
Hamm *et al*. 2002[16]	Prospective comparative 3B	109	73.0	13.7	M: 76, F: 33 Age: 20-84 (mean 49 years)
Mulkens *et al*. 2007[17]	Prospective quasi randomised 4	300 (150 in LDCT group and 150 in SDCT group)	52.7	15-16	LDCT group M: 97, F: 53 Age: 18-87 (mean 50.23 years) Mean BMI 24.87 SDCT group M: 91, F: 59 Age: 22-90 (mean 52.5 years) Mean BMI: 26.71
Kluner *et al*. 2006[18]	Prospective comparative 4	142	72.0	14.8	M: 74, F: 68 Age: 18-83 (mean 47 years)
Tack *et al*. 2003[19]	Prospective comparative 4	106	36.0	12.0	M: 53, F: 53 Age: 15-84 (mean 45 years) Mean BMI: 26.2

BMI=Body mass index, KUB=Kidneys, ureter and bladder, LDCT=Low-dose CTKUB

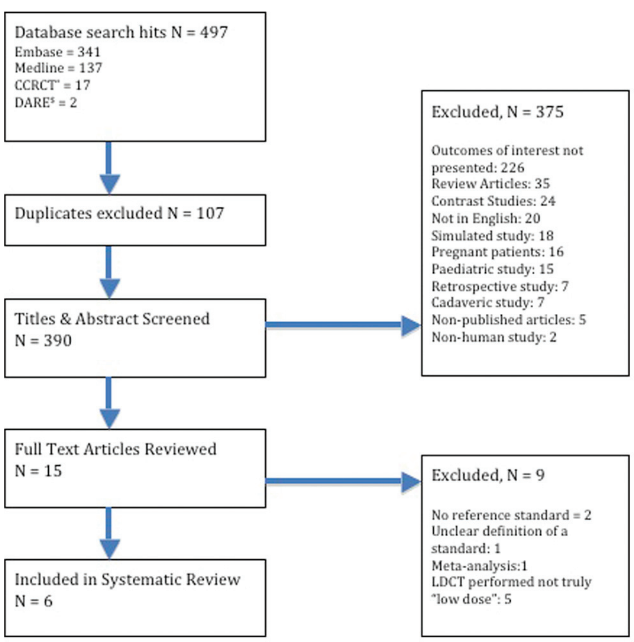

Figure 1: Flow chart showing literature retrieval process

stone prevalence of 52.7-87.9%. All patients presented with acute flank/lumbar pain suspicious for renal colic or were being followed-up for known urolithiasis. All studies were prospective, published in English language between 2002 and 2008 and compared the diagnostic accuracy of LDCT (<3 mSv) to a reference standard (either standard dose CT or a composite reference consisting of other imaging modalities and clinical follow-up) [Table 3].

Meta-analysis of the extracted data was not performed because there was a significant heterogeneity among the 6 studies in terms of the reference standards used and outcome measures examined.

Quality evaluation of included studies

Overall, the quality of the included studies was modest, as barring the three Level 1 studies; the remainder of the studies have methodological flaws, mainly due to the use of a composite or weaker reference standard. In particular, some components of the reference standards used, such as the presence or absence of microscopic haematuria[20] plain abdominal film[21] or ultrasound scan[22] are of questionable value in diagnosing urolithiasis. Moreover, in some of the included studies, different investigation modalities were applied to different patients, which may have been influenced by the results of the initial CT scan, making it highly likely that the index test (LDCT) was actually being used as part of the patient work-up [Figures 2 and 3].

DISCUSSION

Since its introduction by Smith *et al.* in 1995 as a means of detecting urolithiasis,[5] non-contrast abdominal/pelvic

Table 3: Imaging technique and outcomes of the included studies

Study	Low dose CT used	Reference standard E_m: Effective dose male E_f: Effective dose female E: Effective dose	Sn and Sp	PPV and NPV	Biases
Kim *et al*. 2005[14]	Siemens Somatom plus 4 MDCT, 50 mAs, 120 kV, collimation 5 mm, recon slice 5 mm, Pitch 1.5 E_M 1.6 mSv; E_F: 2.1 mSv	SDCT 260 mAs and other tests E_M: 7.3 mSv; E_F: 10 mSv	Sn 93-95% (68-79% for stones <2 mm) Sp 86%	PPV 0.98-0.99 NPV 0.63-0.71	Spectrum bias
Poletti *et al*. 2007[15]	Phillips MX 8000 4 MDCT, 30 mAs, 120 kV, recon slice 5 mm, Pitch 1.25 E_M: 1.6 mSv; E_F: 2.1 mSv	SDCT 180 mAs, 120 kV, recon slice 5 mm, Pitch 1 E_M: 9.6 mSv; E_F: 12.6 mSv	Sn 97% Sp 96%	PPV 0.99 NPV 0.88	Spectrum bias
Hamm *et al*. 2002[16]	Siemens Somatom plus 4 MDCT, 70 mAs, 120 kV, collimation 5 mm, Pitch 2 E_M: 0.98 mSv; E_F: 1.5 mSv	USS in all. Retrograde ureteropyelogram in 51 (47%) and clinical course	Sn 96% Sp 97%	PPV 0.99 NPV 0.90	Spectrum bias, unclear criteria, delay in index and reference test, partial verification
Mulkens *et al*. 2007[17]	6 MDCT, 51 mAs, 110 kV, Pitch 1.3, Collimation 1 E_M: 1.29 mSv; E_F: 1.78 mSv	Multiple, other imaging, KUB/USS/URS/IVU/clinical follow-up E_M: 2.48-4.37 mSv; E_F: 3.51-4.57 mSv	Sn 96-98.6% Sp 90.2-93.5%	PPV 0.9-0.94 NPV 0.96-0.99	Unclear criteria, inappropriate reference test, delay in index and reference test, 59% lost to follow-up
Kluner *et al*. 2006[18]	Toshiba 16 MDCT, 20 mAs, 120 kV, recon slice 5 mm, Pitch 1.43, Collimation 16, gantry rotation 0.5 s E_M: 0.5 mSv; E_F: 0.7 mSv	Combination of clinical and follow-up imaging including SDCT, USS, MRI or a combination of retrograde pyelography and KUB	Sn 97% (CI 92-99%) Sp 95% (CI 83-99%)	PPV 0.98 NPV 0.93	Spectrum Bias, inappropriate reference test, unclear criteria, delay in index and reference test, 59% lost to follow up
Tack *et al*. 2003[19]	Siemens Somatom plus 4 MDCT, 30 mAs, 120 kV, 2.5 mm collimation, pitch 1.5 and additional imaging at 60/120 mAs, recon slice 3 mm E_M: 1.2 mSv; E_F: 1.9 mSv	Combination of clinical, surgical and radiological investigations	Sn 90-95% Sp 94-100%	PPV 0.9-1.0 NPV 0.93-0.98	Unclear criteria, inappropriate reference test, delay in index and reference test, partial verification

KUB=Kidneys, ureter and bladder, PPV=Positive predictive value, NPV=Negative predictive value, Sn=Sensitivity, Sp=Specificity, CI=Confidence interval, SDCT=Standard-dose CTKUB, LDCT=Low-dose CTKUB, URS=Ultrasonography, MRI=Magnetic resonance imaging USS=Ultrasound scan, MDCT=Multi-detector CT, KUB=Kidneys, ureter and bladder, IVU=Intravenous urography, CT=Computed tomography

computerized tomography has become the accepted gold standard for the evaluation of patients presenting with suspected renal calculi. However, there are concerns regarding the significant amounts of ionizing radiation that this exposes patients to, particularly as urolithiasis is a disease predominantly affecting young people, with a recurrence risk of 50% in 5-10 years and 75% in 20 years.[23] The reported effective radiation dose from a single standard radiation dose CTKUB of 4.3-14 mSv,[16,19] therefore accumulates as additional CT scans are performed to monitor disease recurrence, stone migration, spontaneous stone passage and the outcome of any stone-treating intervention. Ferrandino *et al*.[24] looked at the total radiation dose received by 108 patients, from imaging studies related to stone disease, over a 1-year period following an acute stone event and found that 20% received a potentially significant radiation dose (>50 mSv). Optimization of scanning techniques to achieve maximal diagnostic imaging quality at the lowest possible radiation dose has therefore become crucial.

The present review found that reducing the radiation dose of CTKUB in this way has little impact on the diagnostic accuracy of the scan, maintaining a high sensitivity of 90-97% and a specificity of 86-100%.[14-19] Kim *et al*. and Poletti *et al*. directly compared LDCT with standard-dose CT and both concluded that the investigation has high sensitivity and specificity for diagnosing urolithiasis when stone size is at least 2 mm[14] or 3 mm.[15] Given that stones < 5 mm have a 68% (95% confidence interval 46-85%)[25] chance of spontaneous passage, one can argue that the ability to detect stones <2 mm in size is clinically insignificant. However, according to Poletti *et al*.,[15] when considering optimal stone treatment based on the results of a LDCT, clinicians

	Representative Sample?	Clearly described selection criteria?	Acceptable reference standard?	Acceptable delay between tests?	Partial verification avoided?	Differential verification avoided?	Incorporation avoided?	Adequate index test description?	Adequate reference test description?	Index test blinded to reference standard?	Reference standard blinded to index test?	Clinical data available as in practice?	Uninterpretable results reported?	Withdrawals explained?
Kim et al. 2005[14]	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	?	Y	N
Poletti et al. 2007[15]	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Hamm et al. 2002[16]	N	N	Y	N	Y	N	?	Y	Y	?	?	Y	Y	Y
Kluner et al. 2006[18]	?	N	N	N	Y	N	?	Y	Y	Y	?	Y	Y	Y
Mulkens et al. 2007[17]	Y	N	N	N	Y	N	?	Y	Y	Y	N	Y	N	Y
Tack et al. 2003[19]	Y	N	N	N	Y	N	?	Y	Y	Y	?	Y	Y	Y

Figure 2: Risk of bias summary: Review authors' judgments about each risk of bias item for each included study

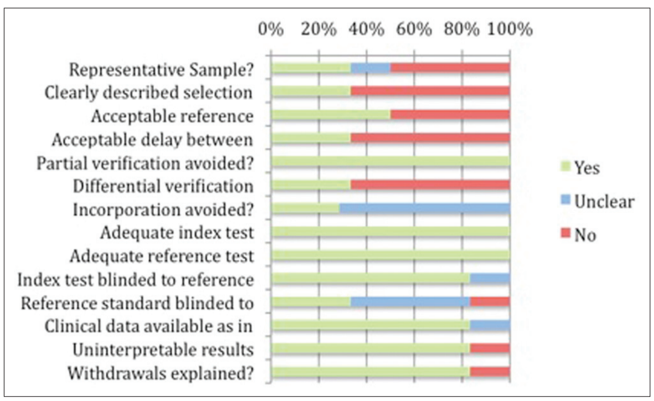

Figure 3: Overall risk of bias graph: Review authors' judgments about each risk of bias item presented as percentages across all included studies

should bear in mind that the size of calculi on LDCT may vary by ± 20% compared with standard-dose CTKUB (SDCT) results. However, there is evidence from a porcine kidney phantom study that contradicts this view.[26] The overall detectability and measured size of calculi using CT may therefore also depend upon their chemical composition.[27,28]

Clinicians may also need to consider the body habitus of their patient before requesting a LDCT scan; Hamm *et al.*[16] reported that the obesity appeared to significantly reduce the ability to accurately diagnose stones in 2 patients with a BMI > 31 kg/m^2. Tack *et al.*[19] noted similar findings with only 1 out of 6 patients with a BMI > 35 kg/m^2 being accurately diagnosed using a low-dose scan. Furthermore, Poletti *et al.*[15] reported that LDCT achieved 95% sensitivity and 97% specificity for detecting ureteral calculi in patients with a BMI < 30 kg/m^2, but only a 50% sensitivity and 89% specificity in those with a BMI ≥ 30 kg/m^2. Interestingly, a more recent cadaveric simulation study carried out by Heldt *et al.*[29] using 3 cadavers of increasing weight/BMI found that although increasing adiposity negatively affected the diagnostic accuracy of ultra-low dose CT (<1 mSv) in detecting ureteral calculi, the sensitivity and specificity of ultra-low dose CT for detecting ureteral calculi was also decreased in underweight cadavers; presumably due to a lack of perinephric and peri-ureteral fat to help delineate the ureters from surrounding structures. However, there was no significant difference in sensitivity and/or specificity at radiation doses of 2 mSv or more, which would still constitute a "low-dose" scan using our definition. In other words, low-dose protocols can still be used for underweight and overweight patients without jeopardizing stone detection.

In Hamm *et al.* study,[16] the only other diagnostic problems occurred in the distal third of the ureter, when small stones with little associated hydronephrosis were missed, i.e. stones with a high likelihood of spontaneous passage. They therefore concluded that all clinically significant stones were correctly detected by LDCT.

The validity of the results of a systematic review is dependent on the quality of the included studies, including selection of patients and inclusion criteria. The studies included were all prospective, human studies, two of which were comparative studies, directly comparing SDCT to LDCT.[14,15] Evidence provided by the remainder of the included studies is weaker due to the aforementioned limitations of using a weaker and/or composite reference standard. However, it is ethically difficult to justify performing a study, which directly compares SCDT with LDCT as this inherently results in exposing patients to excessive radiation. Overall this review has at least one level 1A and two level 1B Levels of Evidence according to CEBM.[13] No study evaluated cost analyses.

One major advantage of unenhanced CT in patients presenting with acute flank pain, is its ability to provide the alternative diagnoses for the pain in the absence of stones. However, perhaps another limitation of this review is that the two Level 1B studies by Kim *et al*.[14] and Poletti *et al*.[15] seem to have a very high prevalence for urolithiasis (87.9% and 80.8% respectively) and a low prevalence for alternative diagnoses (4.8% and 7.4 and respectively) which may reflect a bias in recruitment against those with higher diagnostic uncertainty. Besides having a better sensitivity and specificity compared to IVU or ultrasonography and pain KUB XR, it can also detect radiolucent stones and help determine stone density, which can help predict treatment success.[2]

Further human studies are needed to evaluate the effect of body weight on the sensitivity and specificity of low dose protocols to detect stones since the diagnostic accuracy of LDCT must be demonstrated across the full spectrum of patients before the widespread adoption of low-dose protocols can occur. Furthermore, body habitus is frequently described in terms of body weight and BMI, several studies have suggested that alternative body measurements such as body weight and circumference may be superior in determining effective radiation doses to ensure diagnostic accuracy.[30] Future research efforts should therefore focus on larger prospective, randomized control trial studies, using validated composite references standards to produce clinically applicable results and to establish clinical criteria for when to perform a LDCT.

CONCLUSIONS

The use of low-dose CTKUB is a safe, sensitive and specific imaging modality for patients presenting with acute loin pain and offers the benefit of significantly lower ionizing radiation exposure compared with conventional CT. LDCT may miss some small stones (<3 mm), especially in obese patients (>30 kg/m^2); however, the clinical significance of this is arguable given that stones up to 5 mm in size have a high rate of spontaneous passage, and even in the obese group LDCT seems to identify most alternative pathologies.

With at least one level 1A and two level 1B studies supporting the use of LDCT in the diagnostic work-up of acute flank pain, there is Grade A recommendation for its use as the first line investigation in suspected renal colic, particularly in non-obese patients.

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